Insulating Biomaterials N01-NS-2-2347

Ninth Quarterly Progress Report October-December, 2004

National Institutes of Health

National Institute of Neurological Disorders and Stroke

Neural Prosthesis Program

InnerSea Technology

1 DeAngelo Drive
Bedford, MA 01730

Contributors:

Dave Edell, PI

Robyn Edell, Testing

Sean Sexton, Instrumentation and Software

Ying-Ping Liu, Assembly and Testing

Karen Gleason, Chem Eng (MIT)

Shannan O'Shaughnessy, Grad Student, Chem Eng (MIT)

The goal of the Insulating Biomaterials work is to identify and evaluate materials, coatings, and assembly techniques suitable for protection of integrated circuit devices being considered for neural prosthetic applications.

Workshop on Neural Interface Technology

The workshop presentation for 2004 is appended to this brief report as it is a fairly up-to-date summary of current results which were compiled during the first half of this quarter.

Instrumentation Systems

Accelerated detection of degradation is the main tool for studying materials for implantable devices. The new Passivation Test System consists of 4 major components: the Tube Top, the Measurement Unit, the Data collection Unit, and the Calibration Unit. These components are described below. Basically, as illustrated in Figure 1 the device to be tested is placed into the saline soak tube.

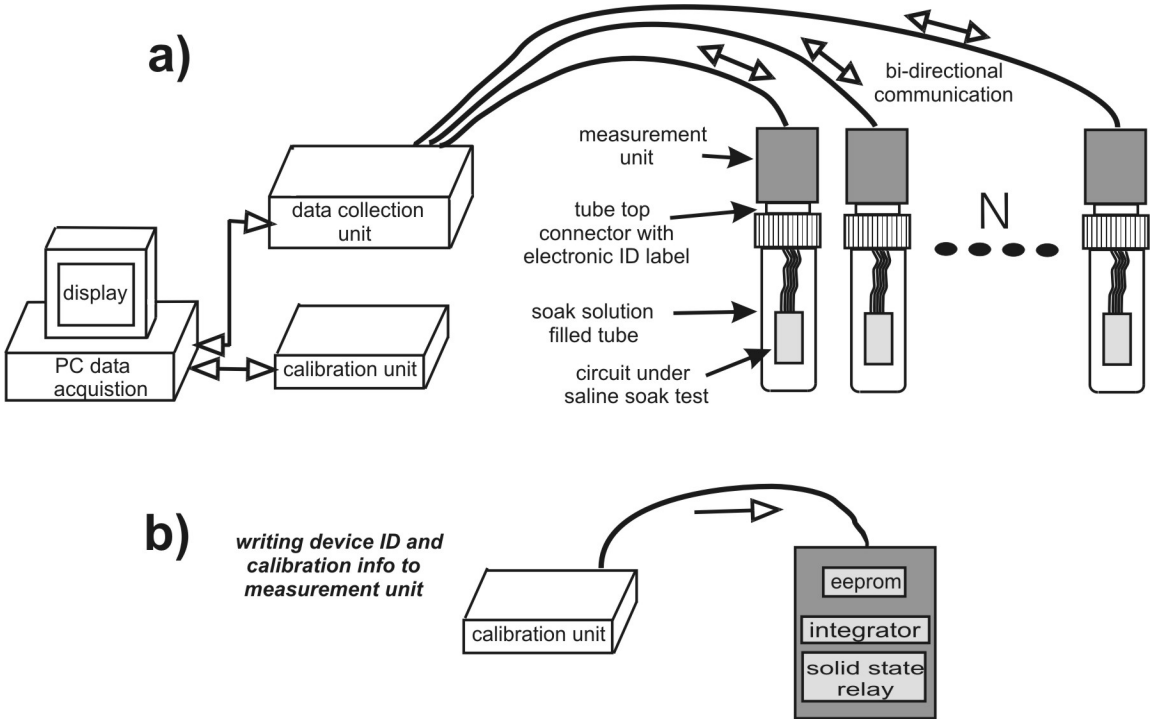

Figure 1: Cartoon showing basic elements of new test system.

1) the Tube Top - This provides: a physical attachment point for the device under test; the electrical connections to the system; and an EEPROM that

contains information about the particular device in that is under soak test in that respective tube.

2) the Measurement Unit - This contains: the analog circuitry required to perform the measurement; a calibration check unit; a continuity tester for triple track devices; and another EEPROM which contains required calibration information.

3) the Data Collection Unit - This accepts the data (consisting of timing signals) from the measurement units, converts them into leakage values, and transmits those values to a host computer.

4) the Calibration Unit - This is a standalone unit that is used with each device before any testing at all is performed, and it is normally used only at the onset of testing. Thus, if a device is tested each day for 100 days, the Calibration Unit is “hooked” up to Measurement Unit at the start of day 1 so that device identification data can be downloaded to the EEPROM that is located on the Tube Top, along with the calibration information particular to the device under test and that will be needed for the Measurement Unit to interpret the measured parameters for every succeeding test day.

Recent Results:

As with the previous quarter, this quarter was spent on bringing the new Passivation Test System online. Currently, the focus is on the calibration board/measurement unit relationship. The firmware for the microcontroller on the calibration board is complete and stable. Minor revisions to this firmware may be made in the future to improve functionality, but at this point it appears to be at an excellent operational level. Two design flaws were discovered on the rev 3 measurement unit (rev 1 used the ACF2101BU integrator from TI which was deemed unsuitable, rev 2 changed the integrator to the IVC102 from TI – This version was never fabricated, rev3 uses the IVC102, and also includes Omron solid state relays). The first flaw was in the connections of the connector that attach to the test device. The configuration as it stood would not allow for continuity testing of the test device. The second flaw was the connections to the

Omron relay. The pin wiring was transposed in such a way as to make the relay inoperable. This problem did not surface until the calibration resistors were added. Once they were installed, the relay caused these resistors to affect the measurement of the test device. The board was modified to overcome these problems, and re-establish the desired functionality. In addition the voltage dividers which generated the reference voltage for the integrator reset were replaced by precision references, to improve the system accuracy.

With the measurement unit and calibration hardware and firmware now operating properly, attention has turned to the host computer software and user interface. Agilent Vee Pro 7 is being used to create the host software for the calibration system, and this will be used for the main system as well. The software will allow the user to read and write the test device information to the device memory, and to calibrate the measurement unit.

The process of completing the calibration software is now underway. Once this is complete, the focus will be on creating the firmware for the data collection unit, much of which will translate directly from the calibration unit, and then the main test software package

Animal Implant Testing

The focus of animal implant testing has been to develop a support electronics and telemetry system for long term monitoring of leakage currents for implantable device evaluations. The most promising assemblies have been based on Liquid Crystal Polymer (LCP) substrate flex circuits. This material has been exhibiting good long term soak performance in saline solutions and has become available for testing in this project through long term collaboration with Foster-Miller, Inc. A variety of test circuits were designed and implemented with LCP substrates. All are based on transducing signals to small (pico-ampere to micro-ampere) currents, and then using a current integrator to generate a pulse train where the time between pulses is proportional to the current. It is important to construct these circuits with sensitive high impedance nodes to challenge the encapsulation system which will allow early detection of encapsulation failure.

With this base system, it is straightforward to implement various sensors such as Inter-Digitated Electrode (IDE) testers, battery monitors, temperature monitors, and bioelectric signal amplifiers. All of these were implemented to exercise the design, assembly, and testing to ensure that when the CMOS self-test circuits previously developed were next implanted (the main goal of most of this work), the long term testing results would be dominated by the CMOS sensors rather than the support battery and interconnects.

Recent Results:

One LCP hybrid circuit is still functioning (over 1 year implanted) from the series implanted over the past year. All other devices have now failed. The surviving circuit, shown in Figure 2 simply monitors the current through a 470kΩ thermistor, encodes the current into a pulse interval modulated data stream, and transmits the data optically across the skin.

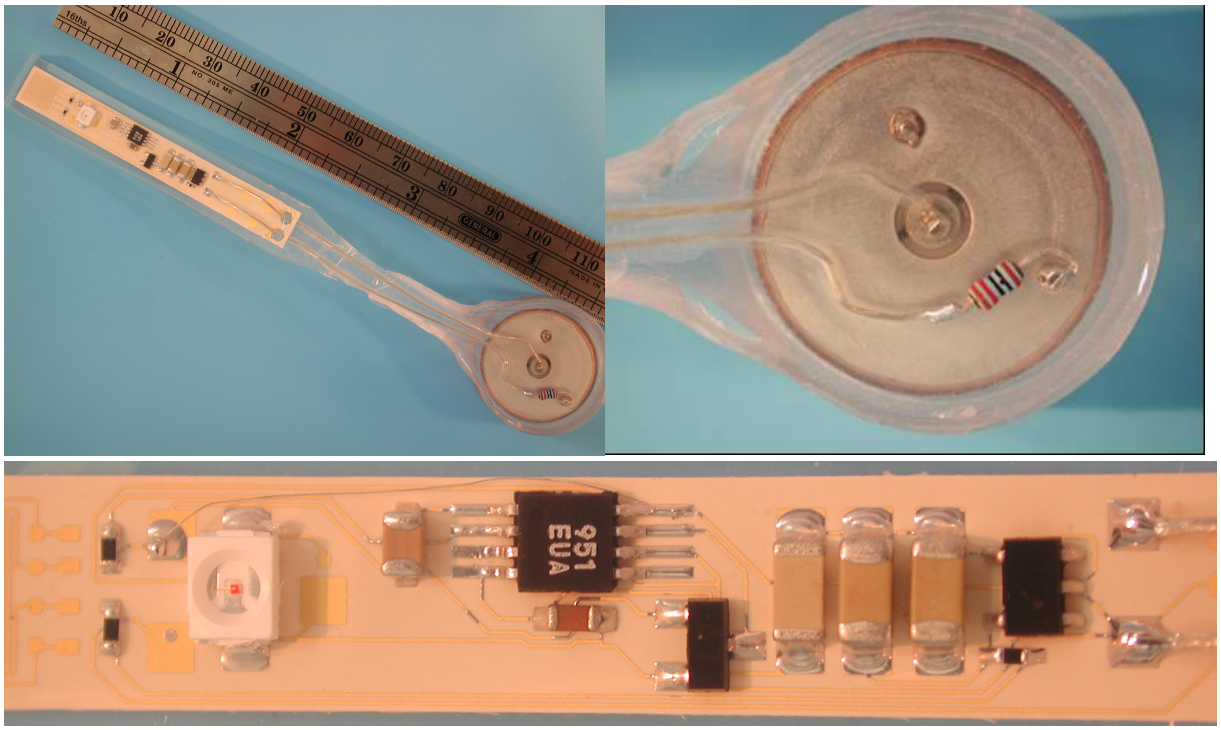

Figure 2: Temperature monitor circuit. 470kΩ thermistor located near the LED transduces temperature into interpulse intervals optically transmitted. Device shown was soaked 52 days in saline prior to photographs, and then implanted October, 2003. Unit is still functioning. Discoloration of glass feedthru surrounding battery anode is worrisome, but so far has caused failure.

Analyses of the failed circuits all show corrosion at the interconnect solder attachments. At the present time, it is not clear how this is happening in view of the somewhat excessive cleaning procedures now in place. These failures will be further investigated in the next quarter, and results compared with triple track devices assembled with similar procedures.

Some devices, when removed following implantation, become cloudy. While not known for certain, this may be related to uptake of Betadine that was used for a time prophylactically to ensure sterility of the implants. An example of such an effect is shown in

Figure 3: Apparent uptake of Betadine used prophylactically may have caused cloudiness shown here.

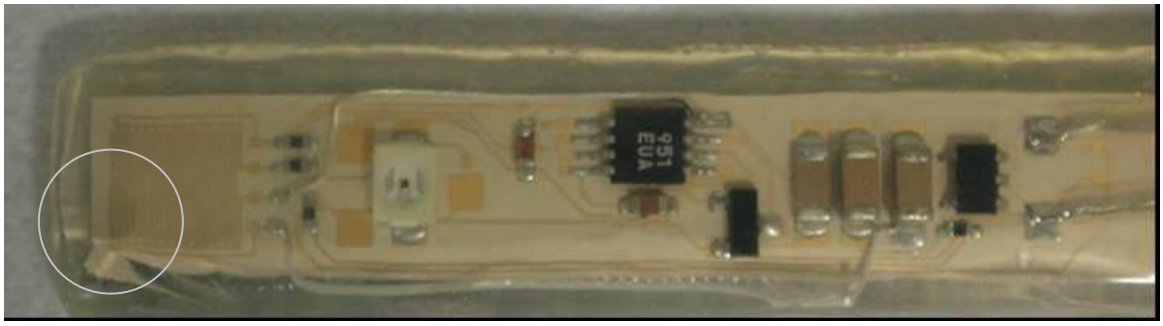

Figure 4: Device of Figure 3 after sitting in room air for days. failed due to apparent local contamination or very small loss of adhesion over IDE monitor at end of device.

A new set of LCP substrate hybrid circuit test devices will be fabricated and implanted next quarter incorporating the improved assembly procedures and materials identified over the past year.

Peel Testing

A rapid screening method for new materials and for testing variations in materials and assembly techniques was vitally needed as the IDE tests were exceedingly costly in time, and difficult to accomplish without investing even more to assemble sets of devices. New materials and new methods are unlikely to work , and require substantial investment to test with the IDE methodology (based on years of experience thus far) so the rapid screening test could greatly accelerate progress by allowing us to focus on the promising pathways.

Accordingly, a peel test was developed. The assumption behind the use of the peel test is that if the bond between the encapsulant and surface being protected weakens over time, or is insufficient to begin with, then the candidate encapsulant is probably not a good choice for long term protection of an implantable integrated circuit. Or, it may be that the material is indeed a great material, but will only work if a method of adhering it to the substrates is developed (fluoropolymers for example). Since the force of adhesion necessarily must depend on both the density of bonds, and the strength of the bonds, it seems that this is an expedient measure to screen the many possible cleaning, surface preparation, adhesion promotion, methods and encapsulants prior to long term, tedious, IDE testing. However, just passing the peel test does not

indicate that the material is useful for these applications. Rather, it may indicate that the material has sufficient promise to warrant further testing.

The basic structure used is a flat plate of glass or quartz to which is bonded the material of interest. Glass or quartz are used since the outer layer of all CMOS integrated circuits likely to be used have at least a monolayer of silicon dioxide on the surface. Glass was used because it is inexpensive (microscope slides) and allowed development of the methodology. Quartz slides are used for definitive testing, as glass substrates have high ionic concentrations not found in silicon devices.

To ensure that the peel begins at the interface, thin Kapton tape stripes are fixed to the quartz slides at 5mm intervals prior to coating with the material of interest. A fiberglass tape is embedded in the material of interest for attachment to the puller, and the assembly is cured appropriately and placed under phosphate buffered Ringer's fluid for long term soak testing. Each peel test consists of pulling the tape 5mm (space between Kapton stripes). The peak peel force is taken as the data point for that peel (in a comparison of average peak force vs peak force, peak force exhibits less variation and does not involve any subjective estimates).

While this is somewhat slow work, it is much more rapid than the glacial pace of the long term soak of wire insulations and IDEs.

Recent Results:

Peel force results repeatability has steadily improved. In order to minimize the micro-bubble effect shown in earlier progress reports, 3 approaches were taken.

1. Vacuum De-airing: Attempts to vacuum de-air the materials prior to curing were not successful. The viscosity of MED4-4220 silicone (a representative 2 part platinum catalyzed material) was too high thereby preventing bubbles from growing and bursting. Vibration was accomplished little. Relatively short pot life further exacerbated the problems.

2. Centrifuge: Centrifugation compacts the silicone and essentially squeezes the air and moisture out of it during cure. This approach was relatively effective, but was difficult to accomplish due to the limited pot life. However, one version of samples made with centrifugation at over 5,000 rpm in a 6" centrifuge tube for 3 minutes yielded a 90^{o} average peel force of over 2,800g/cm relatively consistently.

3. Lower Viscosity Silicone: In order to lengthen the cure time, and lower the viscosity to allow vacuum de-airing, a custom formulation (CSM4220-3) was developed by Nusil, Inc (Carpenteria, CA). This material readily de-aired in just a few minutes. The lower viscosity facilitated infiltration into the stranded wire and fiberglass used in various test structures. While this totally eliminated the bubbling problem, the material is relatively weak due to the reduction in silicone filler. Thus when fiberglass tape peeled, the material simply separated at a relatively modest peel force (~100-200gms). With such low break strength, it is difficult to challenge the bonded interface since the material separates before generating high peel forces.

While examining the causes of low peel forces for the custom silicone, it was observed that infiltration of the fine fiberglass was not consistent. A coarser weave fiberglass was procured and tested. Initial results indicate that more consistent results with peel forces in the 2300-2500gm range were obtainable with the MED4-4220, and minimal micro-bubbling was observed. This may have been due to better wetting and penetration of the coarser weave fiberglass. Use of this coarser fiberglass also increases the upper limit of peel strength for the tape itself, which now allows peel forces of over 4,000gms without tearing of the tape.

Now that the peel test is relatively well developed, investigation of the adhesion promoters will begin next quarter.

HFCVD of Silicones

In order to apply the materials being identified as good encapsulants for long term implantable devices to fine microstructures such as micro-fabricated

electrode arrays and micro-wires, vapor phase deposition techniques have been explored extensively. At the beginning of this work, when a variety of materials were screened for long term insulative properties under voltage biased, saline soak conditions, it became clear that fluoropolymers were much superior to other materials such as polyimides, urethanes, and parylenes for very long term survival. Chemical Vapor Deposition (CVD) methods were the only ways known to afford the possibility of creating thin (<10μm), conformal, and pinhole free coatings. Plasma Enhanced Plasma Enhanced Plasma Enhanced CVD (PECVD) and Hot Filament CVD (HFCVD) techniques were developed for depositing fluoropolymers. While these materials would survive indefinitely under saline soak and in long term soaks in animals, it was not easy to adhere these materials to silicon dioxide surfaces (silicon dioxide is the outer dielectric layer of essentially all micromachined devices other than micro-wires). In addition, micro-defects in wire coatings produced by these methods made it difficult to rely upon them for micro-wire applications. While not abandoned, it became apparent that a better adhering material with adequate electrical properties might be superior to the CVD fluoropolymers. PECVD silicone depositions resulted in materials that adhered very well to silicon substrates, and also coated wires, but were too brittle from cross-linking induced by the plasma. However, HFCVD produced silicone materials showed more promise. A peroxide catalyzed reaction with a cyclic silicone monomer has produced the most controllable reaction and is currently being pursued.

Recent Results:

Work over these three months has focused on four main areas:

1) Preparation and presentation of materials for Neuroprosthetics workshop.

2) Evaluation of material electrical properties

3) Investigation of reaction kinetics in preparation for publication of research

4) Interviewing and training of undergraduate research assistant

Work continues on evaluation of the tertbutyl-peroxide initiated trivinyl-trimethyl-cyclotrisiloxane polymer. Primary investigation has focused on the evaluation of electrical properties of thin films of the material including resistivity and long term durability under saline soak. Initial results are very promising, with films deposited at optimized conditions showing resistivity on the order of 10^{15} Ohm-cm. In addition, all prepared samples at these conditions have proven to be resistive, with no flaws or holidays. Samples have also now been under soak for >6 months with no degradation of electrical properties.

In addition to the evaluation of material properties, work is ongoing to better understand the reaction kinetics of the polymerization and to quantify reaction activation energy, heat of adsorption and degree of polymerization. This data will be utilized to help describe the polymerization in future planned publications. Much of the data collection for this effort is being performed by a new undergraduate research assistant, Mei Gao. Mei was selected after interviewing multiple possible candidates. She has been trained to use the CVD reactor and thin film analysis equipment in the Gleason lab. It is anticipated that she will continue to work on the project for at least the next semester. She will also be assisting in the initial stages of moving from a monopolymer to a copolymer to better optimize deposition conditions for formation of thin films on three dimensional substrates. Current filament temperature requirements inhibit deposition on substrates not indirect contact with the reactor stage due to overheating.

Lastly, much time has gone in to preparation of presentation materials. A poster describing the work to date was presented at the Neuroprosthetics workshop in Bethesda in November. In addition, an extended abstract of the work has been accepted for oral presentation at the American Chemical Society conference in March 2005.

SEE POWER POINT PRESENTATION